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EXAMINER	
LIU, SAMUEL W	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,121	SIDELMAN, ZVI	
	Examiner	Art Unit	
	Samuel W. Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-283* is/are pending in the application.

4a) Of the above claim(s) *1-12,65-96 and 101-283* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-64 and 97-100* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-283 are pending.

Note that he applicant's request filed 2/2/05 for extension of time of two months has been entered.

Election/Restrictions

Applicant's election (filed 2/2/05) of claims 13-64 and 97-100 (see the following statement) is acknowledged. Because applicant did not expressly point out that the election is made with transverse, the election has been treated as an election without traverse (MPEP § 818.03(a)). Note that this election is based on the Examiners' agreement with Applicant as to rejoining Groups 3-8 and 15 (claims 13-64 and 97-100) (see the Interview Summary mailed 9/17/04). Therefore, the elected claims 13-64 and 97-100 with the elected the SEQ ID NO:4 sequence (see page 3 of the applicant's response (filed 2/2/05) to the restriction requirement mailed 7/1/04) are examined in this Office action.

In the response (filed 2/2/050, applicant asserts that the election of the sequence of SEQ ID NO:4 for examination is a species election. As stated in the Office action mailed 7/1/04, Examiner here emphasize that the said election is not a species election but rather the additional election requirement under 35 USC 121, and that the peptide sequences set forth in the claims of the invention are structurally (in both composition and sequence) distinct/different from one another; and thus, they patentably distinct from one another.

Claims 1-12, 65-96 and 101-283 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention for the reasons stated

above and in the restriction requirement. Therefore, claims 13-64 and 97-100 with the elected SEQ ID NO:4 sequence are under examination to the extent that they are drawn to the elected invention.

IDS

The references of the IDS filed 9/1/04 have been considered by Examiner. Yet, it should be noted that inasmuch as the full-text copies of the non-patent literatures, i.e., Chabance *et al.* and Coste *et al.*, have not been submitted (only the copies of abstract pages thereof are submitted), Examiner has specified "(*abstract*)" at the ends of citations of the above-mentioned literatures.

Specification/Claim/ Objections

The disclosure is objected to because of the following informalities:

(1) On page 21, line 21, "FITC" should be spelled out in full for the first instance of use. See also, page 21, line 22, "RPE", and page 62, line 10, "BSA".

(2) The drawings are object to because of the following issues. In Figure 2a, the Table above the plot of Figure 2a has not been appropriately labeled. Se also Figure 3a, 3b, 3c; Figure 4; Figure 5a (the left Table of the Figure 5a plot); Figure 8; and Figure 9. Figure 11 contains two Tables both which should be labeled. The Figure 15 appears to contain two Tables which should also be labeled. And, In Figures 17 and 18, there are the Tables depicted with "X" and "Y" values wherein identity of the values is unclear; do these values refer to the values of the "X"-axis (e.g., PLT x 10 /ml) and the "Y"-axis (Days), or the values of "X" and "Y" (which has not shown on the drawings)? The clarification of this regard is required.

On page 2, the definition for oS1 casein is not clear. Note that, currently, "αS1-casein" is widely accepted (see Rincon et al. reference (*J. Anim. Breed. Benet.* (2003) 120, 331-337). Does the phrase "oS1 casein" in this application actually refer to as the "αS1-casein"? Clarification of this regard is required. It was noted that Applicant also files Application No. 10/788400 wherein the phrase "αS1-casein" rather than "oS1 casein" is recited throughout the specification. It appears that the "αS1-casein" and the "oS1 casein" are the same composition.

In claim 13, "N terminus portion" should be changed to "N-terminal portion". See also claims 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61 and 97.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-64 and 97-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification *neither* describes amino acid sequence (full-length) of the oS1 casein full-length (note that, this description is necessary because, without description of the oS1 casein amino acid sequence, one skilled in the art is unable to determine the amino acid sequence of the N-terminal portion/fragment thereof), *nor* teaches/describes that from which amino acid residue to which residue the said N-terminal portion refers to. For instance, on page 78, lines 22-23, the

specification sets forth that "*the first 5 to 24 amino acids of oS1 casein*", without the Os1 casein full-length sequence, one skilled in the art would not know what is the first 5 to 24 amino acids thereof.

The specification does not describe/teach the core sequence or structural motif(s) which is important for the biological activity of the N-terminal portion *peptide* of the Os1 casein, e.g., stimulating plasma cell proliferation. The "*Experimental Results*" section (pages 71-81) of the specification provides plurality of the Os1 peptides (the drawings do the same) encompassing synthetic peptides or undefined/undetermined (*in sequence*) peptides derived from natural casein, but does not set forth particular amino acid sequences for the claimed methods which are:

– methods of inducing hematopoiesis (claims 13-16);

– hematopoiesis stem cells proliferation (claims 17-20);

– hematopoiesis stem cells proliferation and differentiation (claims 21-24);

– megakaryocytopoiesis (claims 25-28);

– erythropoiesis (claims 29-32);

– leukocytopoiesis (claims 33-36);

– thrombocytopoiesis (claims 37-40);

– plasma cell proliferation (claims 41-44);

– dendritic cell proliferation (claims 45-48);

– macrophage proliferation (claims 49-52);

– methods of treating or preventing thrombocytopenia (claims 53-56); pancytopenia (claims 57-60), and granulocytopenia (claims 61-64); and

– method of augmenting an effect of thrombopoietin (claims 97-100) comprising

administering to a subject a peptide comprising the N-terminal portion of the oS1 casein polypeptide.

The specification sets forth the method of stimulating megakarocyte proliferation (page 78) comprising administering to a subject a peptide comprising the first 5-24 amino acids of oS1 casein. However, the specification does not describe the amino acid sequence of the oS1 casein sequences (Note that there are at least two subtype of alpha casein, i.e., α1-casein and α2-casein which are considered to be most closely related to said "os1 casein" of this application (see page 903, the left column of Kampa et al. [*Biochem. J.* (1996) 319, 903-9080]), one skilled in the art would not know to what casein polypeptide the first 5-24 amino acids refer.

Moreover, the peptide sequences vary from species to species. Thus, the skilled artisan would have not known how to make and use the N-terminal portion of the Os1 casein in order to develop the claimed methods (claims 13-64 and 97-100), and therefore, the skilled artisan are unable to practice the claimed invention.

In addition, the specification neither describes the methods of preventing thrombocytopenia (claims 53-56), pancytopenia (claims 57-60), and granulocytopenia (claims 61-64) comprising administering to a subject a peptide comprising the N-terminal fragment/portion of the oS1 casein, nor provides animal model or/and example in this regard. Thus, applicant is not in possession of the claimed methods.

Therefore, the current disclosure lacks written description.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 13-64 and 97-100 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 13 recites "a peptide derived from an N terminus portion of oS1 casein"; the recitation is unclear as to (i) whether or not the oS1 casein is an αS1-casein polypeptide; (ii) whether or not the phrase "a peptide derived from " refers to (a) a chemical or enzymatic cleavage product of the oS1 casein, or (b) a chemically synthesized casein peptide/polypeptide, or (c) peptide mimetics encompassing any peptide homologues (structurally or/and functionally) to an N-terminal portion of the oS1 casein; and (iii) whether or not said peptide has been isolated or purified from a naturally-occurring casein or/and modified casein or/and synthesized casein. Note that the specification (page 34) provides insufficient definition for this recitation. Also, claim 3 is indefinite because without setting forth sequence identifier (SEQ ID NO:_) for the oS1 casein, the amino acid sequence of the said peptide cannot be determined. See also claims 17, 21, 25, 29, 33, 37, 41, 45, 49, 53, 57, 61 and 97. The dependent claims are also rejected.

Claim 16 sets forth non-elected SEQ ID NOs: 1-3 and 5-25 which are drawn to non-elected invention; thus, re-writing the claim is advised in order to eliminate the subject matters which have been withdrawn from consideration by this Office action. See also claims 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64 and 100.

Claim 94 recites "the effect of thrombopoietin". The thrombopoietin is a humoral factor. The claim recitation does not make it clear that to what biological or/and therapeutic effect the claim refers.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-64 and 97-100 are rejected under 35 U.S.C. 102(b) as being anticipated by Enomoto, A. et al. (*Mol. Immunol.* (1990) 27, 581-586) as evidenced by the known fact that the amino acid sequence (bovine) of αs1-casein polypeptide comprises "RPKHP" (residues 16-20) which is identical to the instant SEQ ID NO:4 (see page 2 of "*NP 851372: casein alpha-S1*" reference in the attached PTO 892).

Enomoto et al teach a process of stimulating hematopoiesis (T-cell proliferation) comprising administering (via injection, see page 582, the left column) to a subject (mice) the αs1-casein peptide. On Figure 3, Enomoto et al. show that the peptide 16-53 of αS1-casein stimulates T-cell proliferation (see also the right column, lines 2-7, page 583). Note that hematopoiesis refers to the formation and development of the blood cells encompassing T-cell proliferation/differentiation. The Enomoto et al. teachings anticipate instant claims 13-14.

In the Enomoto's process, the peptide is synthesized (see the description of Figure 3 and page 582, the right column, the last paragraph), which anticipates instant claim 15.

The peptide is bovine αs1-casein peptide (see abstract). The amino acid sequence (bovine) of αs1-casein polypeptide comprises the residues "RPKHP" (residues 16-20) which has 100% sequence identity to the instant SEQ ID NO:4 (see "*NP 851372: casein alpha-S1*" reference in the attached PTO 892), which anticipates instant claim 16.

Since administering to the subject the above-mentioned peptide would inevitably lead to inducing (i) hematopoiesis stem cells proliferation (claim 17-20), (ii) hematopoiesis stem cells proliferation and differentiation (claims 21-24), (iii) megakaryocytopoiesis (claims 25-28), (iv) erythropoiesis (claims 29-32), (v) leukocytopoiesis (claims 33-36), (vi) thrombocytopoiesis (claims 37-40), (vii) plasma cell proliferation (claims 41-44), (viii) dendritic cell proliferation (claims 45-48), and (ix) macrophage proliferation (claims 49-52), and augumenting an effect of thrombopoietin (claims 97-100), and would also inevitably lead to treating disorders state, e.g., thrombocytopenia (claims 53-56), pancytopenia (claims 57-60), and granulocytopenia (claims 61-64), the above Enomoto et al. teachings thus anticipate instant claims 17-64 and 97-100.

Because structural feature is inherent property of a biomolecule, the said αs1-casein peptide would have the above-mentioned biological activities [see (i) – (ix)]. It is of note that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada* 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

If applicant wish to rebut the above rejection under 35 USC 102(b), applicant must provide factual evidence that the Enomoto et al. peptide comprising the applicant elected SEQ ID NO:4 subsequence does not have the above-said biological activities.

Provisional Rejection - Obviousness Type Double Patenting

Claims 13-64 and 97-100 of this application conflict with claims 7, 9-11, 14-18, 39 and 41-43 of Application No. 10/788400. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 13-64 and 97-100 are provisionally rejected under the judicially created doctrine of obviousness double patenting over claims 7, 9-11, 14-18, 39 and 41-43 of Application No.10/788400. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 7 of 10/788400 discloses the common subject matter as that of the instant claims 53, 57 and 61 because the conditions thrombocytopenia (claim 53), pancytopenia (claim 57), and granulocytopenia (claim 61) belong to blood disease or condition.

Claim 9 of 10/788400 discloses that the administrated peptide is a fragment derived from the N-terminal portion of αS1 (equal to oS1) casein, which is the common subject matter of instant claims 54, 58 and 62.

Claim 10 of 10/788400 discloses that the peptide is a synthetic peptide, which is identical t instant claims 55, 59 and 63.

Claim 11 of 10/788400 is identical to instant claims 56, 60 and 64.

Claims 14-15 of 10/788400 disclose a method of modulating (*including inducing/ stimulating*) hematopoiesis (instant claims 13), hematopoiesis stem cells proliferation (instant claim 17), hematopoiesis stem cells proliferation and differentiation (instant claim 21), megakaryocytopoiesis (instant claim 25), erythropoiesis (instant claim 29), leukocytopoiesis (instant claim 33), thrombocytopoiesis (instant claim 37), plasma cell proliferation (instant claim 41), dendritic cell proliferation (instant claim 45), macrophage proliferation (instant claim 49), which is obvious variation of the instant claims 13, 21, 25, 29, 33, 37, 41, 45 and 49.

Claim 39 of 10/788400 sets forth a method of augmenting the effect of a blood cell stimulating factor comprising administering to a subject the N-terminal portion of the αS1 casein

peptide, which is obvious variation of the instant claim 97. Note that one of thrombopoietin effects (instant claim 97) is stimulating the production of thrombocytes (blood platelets).

Claims 16, 17, and 18 of 10/788400 are identical to (i) instant claims 14, 15 and 16, respectively; (ii) instant claims 18, 19 and 20, respectively; (iii) instant claims 22, 23 and 24, respectively; (iv) instant claims 26, 27 and 28, respectively; (v) instant claims 30, 31 and 32, respectively; (vi) instant claims 34, 35 and 36, respectively; (vii) instant claims 38, 39 and 40, respectively; (viii) instant claims 42, 43 and 44, respectively; (ix) instant claims 46, 47 and 48, respectively; and (x) instant claims 50, 51 and 52, respectively.

Claims 41, 42 and 43 of 10/877400 are identical to instant claims 98, 99 and 100, respectively.

Therefore, the claims of the present application are not patentably distinct from the claims of 10/788400.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

SWL

Samuel Wei Liu, Ph.D.
Art Unit 1653, Examiner
June 21, 2005

JON WEBER
SUPERVISORY PATENT EXAMINER